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Effectiveness of oromucosal medical Cannabis versus placebo in reducing chronic musculoskeletal pain: a systematic review and meta-analysis

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Abstract: Chronic musculoskeletal pain is highly prevalent in the adult population, causing disability and negatively impacting quality of life. Conventional analgesics, including opioids, present risks of dependence and adverse effects. In this context, medical cannabis is proposed as a therapeutic alternative. The objective of this study was to determine the effectiveness of medical cannabis administered via the oromucosal route, compared to placebo, in reducing chronic musculoskeletal pain in adults. A systematic review with meta-analysis was conducted following PRISMA 2020 guidelines and the Cochrane Handbook. The protocol was registered in PROSPERO (CRD42023430465). Randomized controlled clinical trials published between 2012 and 2023 in English, Spanish, and Portuguese were included. Data extraction and risk of bias assessment were carried out by independent and blinded reviewers. Statistical analysis was performed using RevMan 5.4 with random-effects models. Out of 2 398 identified records, five randomized clinical trials were included, with a total of 384 participants with fibromyalgia, multiple sclerosis, and sickle cell disease. The cannabis group showed a significant reduction in pain intensity, with a mean difference of 1.10 (95% CI: 0.65–1.55; $p < 0.00001$) compared to placebo. High heterogeneity was observed ($I^2 = 93\%$), attributed to clinical and methodological differences. The placebo group showed a smaller reduction of 0.43 points. Oromucosal medical cannabis demonstrates greater effectiveness than placebo for the management of chronic musculoskeletal pain in adults. Nevertheless, the heterogeneity of the studies and the limited sample sizes justify the need for additional, higher-quality, and longer-duration clinical trials to confirm its long-term efficacy and safety.

Keywords: Chronic musculoskeletal pain; Medical cannabis; Meta-analysis; Oromucosal administration; Placebo.